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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,883	05/01/2002	Francois Mallet	112062	3896

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,883	MALLET ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/27& 08/01/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 44-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 44-48* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 March 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 9/10/2005
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SD

DETAILED ACTION

RCE

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/26/2005 has been entered. The RCE action follows:

Response to Amendment

This is a response to the amendment filed 06/27/05. Claims 1-37 and 39-43 have been canceled. Claim 38 has been amended. New claims 44-48 have been added. Claims 38 and 44-48 are pending before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 38 and 44-48 are still rejected under 35 U.S.C. 112, first paragraph on the same ground as stated in the previous Office Action, because the specification, while being enabling for detecting the presence of a human endogenous retrovirus W (HERV-W) envelope protein by fusing cells expressing polypeptide of SEQ ID NO:1 or a polypeptide comprising the TM+ Cyt domain at amino acid residues 448-538 of SEQ ID NO: 1 with cells expressing a human neutral amino acid transporte, hATB°, i.e. the RD114/simian type D retrovirus receptor, does not reasonably provide enablement for a method to detect the envelope protein,encoded by any gene

isolated from the chromosomal 7 that comprises any series of 20 amino acids having 95% identity with said TM+Cyt region, wherein the cell contains other cell receptors except hTAB°. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

3. In response to the previous office action, applicants cancel the claims 39-43, amend claim 38, and submit that because the specification's disclosure enables a region of amino acid residues 448-538 as discussed in the interview with the examiner, the newly submitted amendment of claim 38 should overcome the outstanding 112 1st paragraph of enablement rejection.

4. Applicants' argument has been respectfully considered; however, it is not found persuasive because the newly amended claim 38 does not limit the HERV-W polypeptide comprising particular TM-Cyt region of 448-538 of SEQ ID NO: 1, and the broad scope of amended claim read on any sequence comprising any series of 20 amino acids that with about 95% identical with said TM-Cyt regions at amino acids 448-538 of SEQ ID NO: 1 or any evey isolated gene from chromosomal 7 comprising a region located in the TM-Cyt region at amino acids 448-538 of SEQ ID NO: 1.

5. The specification does not provide sufficient evidence to support such broad scope of claim. Instead, applicants' own disclosure shows that it is unpredictable for using any polypeptide comprising any series of 20 amino acids that is at least 95% identical with said TM-Cyt regions at amino acids 448-538 of SEQ ID NO: 1. For example, the fusion protein W/CD46+ comprises amino acid residues from 1-469 and W/R+ fusion protein comprises ENV HERV-W amino acids 1-469, while both of them contain 21 amino acids from the TM-Cyt region of 448-538, none of them is enable to form a fusion (See Fig. 6 and lines 5-30 on page 31).

6. The fusogenic power of the chimeric HERV-W fusion protein can only be produced with a chimeric polypeptide (RD/W) that comprises full length of TM+Cyt region of amino acids set forth of amino acid residue from 448 to 538 (See lines 31-39 on page 31).

7. Moreover, the specification only teach that hATB° is only the cell receptor that mediates the HERV envelope protein mediated fusion. No other receptor has been tested and approved to be involved with the HERV-W envelope protein binding and fusion activities. The receptor that is used by a retrovirus is very critical and identical. For example, it is well know that the receptor CXCR4 is only used by T-tropic HIV-1 T-tropic virus for its envelope protein mediated fusion, but not by M-tropic HIV, whereas receptor CCR5 is only used by M-tropic HIV envelope protein. The specification only teach that hATB° is required for the HERV-W envelope protein mediated fusion. The specification is not deficient for teaching any other receptor is evolved in the fusion. The specification does not provide any guidance for selection any other receptor expect hATB° for the fusion assay.

8. Because the scope of the claims is so broad and applicants failed to provide enough evidence to support the broad scope of claimed invention, and it still renders undue experimentation for a person with ordinary skill in the art. The claims are still rejected.

New Ground Objection and Rejection:

Drawings

9. The informal drawings are not of sufficient quality to permit examination. In the instant case, the drawings lack of illusions in the specification and are labeled with handwritings. Accordingly, replacement drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to this Office action. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action.

10. Applicant is given a TWO MONTH time period to submit new drawings in compliance with 37 CFR 1.81. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a). Failure to timely submit replacement drawing sheets will result in ABANDONMENT of the application.

Specification

11. The disclosure is objected to because of the following informalities: the specification does not contain illustration of the Figures filed with the application. Please prove the illusions for all figures. Appropriate correction is required.

Claim Rejections - 35 USC § 102/103

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 38, 44-48 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Jacobs et al. (US Patent No. 6,312,921B1) for claims 38, 44-45, 47 in light of teaching by Castadna et al. (The J. Experimen. Biol. 1997, Vol. 200, pp. 269-286) or in view of disclosure by Rasko et al. (Proc. Natl. Acad. Sci. USA,

March 1999, Vol. 96, pp. 2129-2134), Tailor et al. (J. Virol. March 1999, Vol. 73, No. 5, pp. 4470-4474) for 46 and 48.

15. The claimed invention is directed to a method of detecting the expression of an envelope protein of a human endogenous retrovirus in cells of a cell culture or a cellular tissue, wherein the envelope protein is HERV-W envelope protein that comprises the TM-Cyt. region of amino acid residues 448-538 of SEQ ID NO: 1. The method comprises the step of co-culturing tow population of cells, one of them expresses said envelope protein, and other expresses human neutral amino acid transporter, i.e. hATB°. The cells can be selected from bone cells, muscle cells, placenta cells, endothelial cells, epithelial cells, glial cells and tumor cells or cells derived from blood vessel (endothelia cells constitutes blood vessel cells according to the histology).

16. Applicants amend claim 38 to have a limitation of allowing said protein to recognize at least one cell surface receptor and further submit that Jacobs et al. do not teach that the fusion they observed do not require any homophilic or heterophilic protein-protein interactions between the cells. Moreover, Jacobs fails to teach the claimed method step of contacting said cells with said protein and allowing said protein to recognize at least one cell surface receptor of said cells. Accordingly, claim 38 (and newly-added claims 44-48) is not anticipated by Jacobs.

17. Applicants' argument and new claims have been fully considered; however, it is not found persuasive because 1). while Jacob et al do not disclose that the Cos cells comprise a cell surface receptor-a neutral amino acid transporter, i.e. hATB°, this receptor is inherently expressed in may human tissues including kidney cell, such as Cos cells in view of disclosure by Castadna et al. (The J. Experimen. Biol. 1997, Vol. 200, pp. 269-286, see 2nd paragraph on page 271 and Table 1 on page 272). They teach that mammalian neutral amino acid transporter including human neutral amino acid transporter, i.e. ATB° is expressed abundantly in kidney cell, and Cos cell is a transfected Africa green kidney cell.

18. 2). The limitation of contacting said cells with said protein and allowing said protein to recognize at least one cell surface receptor of said cell does not seem to be active step because when the cell population expressing the HERV-W envelope is inoculated with other cell population expressing the receptor, the envelope inherently contacts with the receptor because the receptor is not added separately as a free element that independently exist from the

inoculated cells in the fusion assay. Therefore, is does not require any active step of adding the receptor separately from adding the receptor expressing cells to the co-culture system. Therefore, the claimed invention is still anticipated by claims 38, 44, 45, and 47.

19. Or alternatively in view of the disclosure of Tailor et al. or Rasko et al. claims 38, and 44-48 would have been obvious for person with ordinary skill in the art to be motivated using all possible cell types that express a human neutral amino acid transporter, i.e. hATB° to test the fusogenic activity of claimed HERV-W envelope protein absence unexpected result since Jacobs et al. already teach that the disclosed HERV-W envelope protein is able to mediate cell fusion, and Tailor et al. or Rasko et a. identify the receptor for the envelope protein mediated fusion as an allele of a human neutral amino acid transporter, i.e. hATB°, which is wildly expressed in many tissues including all cell types as claims 47-48 drafted (Tailor et al. , Fig. 3 by Tailor on page 4472).

20. As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 38, 44-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blond et al. (J. Virol. Feb. 1999. Vol. 73, No. 2, pp. 1175-1185), Rasko et al. (Proc. Natl. Acad. Sci. USA, March 1999, Vol. 96, pp. 2129-2134), Tailor et al. (J. Virol. March 1999, Vol. 73, No. 5, pp. 4470-4474).

23. The claimed invention is directed to a method of detecting the expression of an envelope protein of a human endogenous retrovirus in cells of a cell culture or a cellular tissue, wherein the envelope protein is HERV-W envelope protein that comprises the TM-Cyt. region of amino

acid residues 448-538 of SEQ ID NO: 1. The method comprises the step of co-culturing tow population of cells, one of them expresses the said envelope protein, and other expresses human neutral amino acid transporter, i.e. hATB°. The cells can be selected from bone cells, muscle cells, placenta cells, endothelial cells, epithelial cells, glial cells and tumor cells or cells derived from blood vessel (endothelia cells constitutes blood vessel cells according to the histology).

24. Blond et al. disclose that HERV-W comprises the full length envelope protein having 100% identical to the claimed envelope protein of SEQ ID NO: 1 (See Fig. 7 on page 1183). Blond et al. conclude that phylogenic analysis of the envelope protein of HERV-W showed that HERV-W is closer to simian type D retrovirus, and avian reticuloendotheliosis retrovirus rather than murine type C retrovirus (See the 1st paragraph on page 1182). Blond et al. do not teach that the envelope protein of HERV-W mediates cell fusion. However, it is well known in the art that all retrovirus envelope protein, especially type D retrovirus envelope protein, is able to mediate cell to cell fusion and form multinuclear of giant cell. This fusion characteristic of type D retrovirus envelope protein is substantiated by Jacobs et al. as described above (See col. 55-57). Blond et al. do not teach that human neutral amino acid transporter, i.e. hATB° is a receptor, which mediates type D retrovirus envelope protein binding and the virus infection.

25. Tailor et al. and Rasko et al. all teach that a sodium-dependent neutral-amino acid transporter is a receptor that mediates Feline and Baboon endogenous retrovirus and simian type D retroviruses infections. The sodium-dependent neutral-amino acid transporter is an allele of hATB° that serve as retrovirus receptor (See Fig. 2 on 2132 by Rasko et al. and abstract by Tailor et al.). Tailor further teach that this receptor is expressed in many tissues, including spleen, lymph node, thymus, peripheral blood lymphocytes, bone marrow, fetal liver, brain, heart, placenta, lung, skeletal muscle, kidney and pancreas et al. (See Fig. 3 by Tailor on page 4472).

26. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references in order to test the HERV-W envelope protein mediated fusion by using the cells expressing envelope disclosed by Blond, to fuse with cells expressing type D retrovirus receptor, hATB° as taught by Tailor et al. or Rasko et al. to establish a method of detecting HERV-W envelope protein using the fusion

characteristics of the HERV-W envelope protein mediated by the receptor of hATB° that is abundantly expressed in may cell types as disclosed by Rasko and Tailor et al. Hence, the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Baoqun Li

Bao Qun Li MD

09/01/2005